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Sub-protocol for assessing Patient Reported Outcomes and Quality of Life in the CONPET study[a]

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STUDY STRUCTURE and COLLABORATORS

Fredrik Schjesvold, Department of Haematology, Oslo University Hospital is sponsor/principal Investigator (PI) of the CONPET study. PI is responsible for conducting the research project, except for the collection of patient reported outcome (PRO) data, which is managed by The Quality of Life Research Center (QLR), Department of Haematology, Odense University Hospital. This include design and description of a protocol for collecting PROs, development of a database to collect and store the PRO data, training of study nurses on how to comply with the PRO protocol. Any questions or problems with the PRO data collection should be directed to the QLR.

[a] NMSG25/16 – THE CONPET STUDY - KRd consolidation in multiple myeloma patients with a positive PET-CT after standard first line treatment" - a phase II clinical trial

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CONPET PROTOCOL SUMMARY

Multiple Myeloma (MM) is the most common hematological malignancy after lymphoms. The overall survival (OS) of patients has doubled in the last 30 years from a median of 2−3 years to 4−6 years in elderly patients, and up to 8−10 years for younger patients. The change in OS is mainly due to autologous stem cell transplantation (ASCT) combined with immunomodulatory drugs and proteasome inhibitors (1-3). However, following first-line therapy, most MM patients experience several relapses in the course of the disease. An important predictor for overall survival is ´time to first relapse´. Recently, it has been shown, that PET-CT before maintenance after first-line treatment is the best predictor for OS (Moreau et al, ASH 2015, abstract 395). Patients with PET-CT positivity are therefore the focus of this study. The primary question to be answered is whether four 28-days cycles of Carfilzomib-Lenalidomide-Dexamethasone (KRd) consolidation after first line therapy can turn PET-CT positivity into negativity.

The primary objectives of the current CONPET trial is to assess the proportion of multiple myeloma patients that are PET-CT positive after standard first line treatment, and, further, how many of these can become PET-CT negative after receiving four 28-day cycles of KRd consolidation treatment. Secondary objectives are to evaluate the effects of KRd treatment on health-related quality of life (QoL) collected through patient reported outcomes (PRO). This protocol describes the rationale, objectives and methods for collecting the PRO QoL data in the CONPET trial.

Table 1. Assessment schedule of health-related quality of life through patient reported outcomes (PRO)

PRO Instruments	Screening	Cycle 1		Cycle 2		Cycle 3		Cycle 4		1 month post Cycle 4	3 month post Cycle 4	End of study at PD
		Day 1	Day 15	Day 1	Day 15	Day 1	Dag 15	Day 1	Day 15			
EORTC QLQ-C30	X	X	X	X	X	X	X	X	X	X	X	X
FACT-PSI	X	X	X	X	X	X	X	X	X	X	X	X
EORTC QLQ-CIPN-20	X	X								X		

mth month; **PD** progressive disease; **EORTC** European Organisation for Research and Treatment of Cancer; **QLQ** Quality of Life Questionnaire; **C30** 30 items; **FACT - PSI** Functional Assessment of Cancer Therapy - Pulmonary Symptom Index, **CIPN20** Chemotherapy-Induced Peripheral Neuropathy-20 items

BACKGROUND and RATIONALE

As a secondary outcome in the CONPET trial, PROs are used to extensively evaluate the health-related QoL during and after consolidation with KRd treatment. Generally, there is a lack of PRO assessments within KRd treatment. As a consequence, patient-experienced side effects (SE) and adverse events (AE) of KRd are not well known. Lenalidomide is a immunomodulatory drug as Thalidomide, and Carfilzomib is a proteasome inhibitor as Bortezomib. Thalidomide and Bortezomib is known to induce peripheral neuropathy in up to 75% of patients treated with these drugs(4) . Further, a large proportion of the patients included in the CONPET trial have been treatedwith Bortezomib as part of their first-line treatment. Thus, KRd treatment is potentially neurotoxic. Though, large phase III randomized controlled clinical trials, using Lenalidomide and/or Carfilzomib as treatment for MM patients, did not find any increase in physician-reported peripheral neuropathy (5-9). However, it is well known, that symptomatic toxicity are underreported by physicians in clinical trials using the Common Terminology Criteria for Adverse Events (CTCAE) (10, 11) . One way to address this, is to collect data directly from patients themselves using PROs. Such PRO is the EORTC QLQ Chemotherapy Induced Peripheral Neuropathy Module 20 (CIPN20) (12). This questionnaire has been validated in MM patients showing that peripheral neuropaty has a negative impact on health-related QoL (13). Thus, it is highly important to investigate and report any occurrence of drug-induced toxicity with the use of PROs. However, chemotherapy induced peripheral neuropathy is yet to be assessed through PROs in MM patients.

Other non-hematologic AEs are pneumonia and dyspnea in MM patients receiving Carfilzomib (14). Similar symptoms are reported in MM patients receiving Lenalidomide alone whereas cardiovascular complications, such as hypertension, pulmonary edema and thromboembolism are potential AEs in MM patients receiving Dexamethasone monotherapy. Finally, lenalidomide in combination with Dexamethasone has shown to increase the risk of venous and arterial thromboembolic events (15). To counteract such symptoms and events diuretic and anti-hypertensive medication are commonly prescribed . Thus, patients that receive either of these

products should be closely monitored in terms of shortness of breath, chest pain, arm or leg swelling.

The aim of this study is to evaluate the effects of Carfilzomib, Lenalidomide, and Dexamethasone (KRd) treatment on secondary PRO endpoints in MM patients with a positive PET-CT after standard first line therapy.

OBJECTIVES

Key:

1. To determine the effects of KRd treatment on shortness of breath throughout the course of treatment (day 1 and 15 in each cycle) using the PRO FACT-PSI.
2. To correlate the peripheral neuropathy scores obtained from the QLQ-CIPN20 with the global QoL domain of the QLQ-C30 at 1 month after completing the KRd treatment
3. To assess the impact of KRd treatment on QoL using the QLQ-C30 global health status/QoL scale at day 15, cycle 4 and 1 month after completing the KRd treatment (1 month after C4) compared to baseline

Secondary:

1. To determine the use of anti-hypertensive and diuretic drugs during the course of KRD treatment (reported by study nurses)
2. To correlate the use of anti-hypertensive and diuretic drugs with shortness of breath using the PRO FACT-PSI
3. To correlate the shortness of breath score using the PRO FACT-PSI with the physical functioning domain of QLQ-C30.
4. To correlate the peripheral neuropathy scores from the PRO QLQ-CIPN20 with the physician reported peripheral neuropathy
5. To correlate the various QLQ-C30 sub-scale scores with the global QoL scale of QLQ-C30

HYPOTHESES

1. Patients report temporary clinically meaningful increased shortness of breath during KRd treatment compared to baseline
2. Due to the course of KRD treatment with cycles of 28 days (21 days of active treatment, seven days pause) patients´ shortness of breath are less pronounced in the last seven days of each cycle.
3. Peripheral neuropathy are increased compared to baseline at the one month follow-up after end of KRd consolidation treatment, but do not significantly effect global QoL (QLQ-C30) compared to baseline values
4. Patients report increased peripheral neuropathy through the PRO QLQ-CIPN20 compared to the physician-reported by by use of the CTCAE
5. Patients show an increase in anti-hypertensive and/or diuretic drug use around the days of KRd treatment
6. Shortness of breath has returned to normal level (baseline values) at the three months follow-up after end of consolidation treatment.
7. Shortness of breath do not affect their self-reported physical functioning as measured with the QLQ-C30 domain.
8. Patients do not report increased clinically meaningful peripheral neuropathy during the course of treatment.
9. Peripheral neuropathy scores using the PRO QLQ-CIPN20 have returned to normal level (baseline values) at three months after starting the last cycle cycle of KRD treatment compared to baseline

METHODS

Eligibility criteria specific to PRO assessment

The critera for in- and exclusion to the assessment of PROs are the same as described in the CONPET study protocol (appendix 1).

Patient Reported Outcome Questionnaires

European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (EORTC QLQ-C30) **(appendix 2)**

QLQ-C30 is a 30-item cancer-specific questionnaire composed by multi-item scales and single-items scales (16). This includes five functional multi-item scales (physical, cognitive, emotional, social and role functioning), three multi-item symptom scales (pain, fatique and nausea/vomiting), a global health status/QoL scale and six single-items assessing additional symptoms (dyspnea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties). Each scale is scored from 0-100, and for the global QoL and functional scales, a higher score means a better functioning, and for the symptom scales, a higher score means higher degree of symptoms (17). The QLQ-C30 is reliable and valid for use in myeloma patients (18). The QLQ-C30 is chosen as it contains scales of physical functioning and global QoL that is to be used to correlate with the other specific PROs.

Functional Assessment of Cancer Therapy - Pulmonary Symptom Index (FACT-PSI) **(appendix 3)**

The FACT-PSI is a 4-item cancer specific symptom index questionnaire developed for patients with lung cancer. Items are equally weighted and scored on a 0-4 scale with total FACT-PSI score ranging from 0-16 (16=asymptomatic)(19). FACT-PSI is cross-culturally translated into Danish, Swedish and Norwegian by the FACIT Measurement System (www.facit.org). FACT-PSI has not been used on MM patients, but is validated on cancer patients receiving second- and third-line

treatment for advanced non-small-cell-lung cancer (20). FACT-PSI is chosen since the time to completion is short (4 items only) and that it is directed specifically towards shortness of breath.

EORTC QLQ Chemotherapy-Induced Peripheral Neuropathy Module 20 (QLQ-CPIN20) **(appendix 4)**

The CIPN20 is a 20-item QoL questionnaire developed to elicit patients' experience of symptoms and functional limitations related to chemotherapy-induced pheripheral neuropathy. The CIPN20 has 3 subscales: a sensory, a motor, and an autonomic subscale.The questionnaire is a valid instrument to distinguish between higher and lower CIPN in MM patients necessery to dedice on dose modification of chemotherapy in clinical practice (13). The CIPN20 is expected to yield a more complete picture of the nature, frequency, and severity of CIPN compared to the more classical, physician-based clinical rating scales.

Treatment schedule

Treatment with intravenous infusion of Carfilzomib is scheduled day 1, 2, 8, 9, 15 and 16 i cycles of 28 days, repeated four times. Dose escalation is performed in cycle 1. Oral Lenalidomide is 20 mg on days 1-21 in each of the four cycles. Oral Dexamethason is 40 mg weekly throughout the study.

PRO Assessment and Time Points

QoL data, using the PROs EORTC QLQ-C30 and FACT-PSI, are obtained at baseline (=screeningsperiod), day 1 and 15 in each treatment cycle, besides 1 and 3 months after the last day of cycle 4 and at “End Of Treatment“ (equal to progressive disease, withdrawel of participant consent, side effects not compatible with continuation in the study or medical conditions that require treatment to be stopped). Data on peripheral neuropathy using the EORTC-CIPN20 questionnaire are to be collected at the following time points; baseline, day 1, cycle 1 and 1 month after the last day of cycle 4 (Table 1).

Administration of the PRO data assessment

A study nurse from each of the participating sites will be responsible for collecting the PRO data. The PRO data will be collected electronically by use of a tablet, handed to the patient, at the outpatient clinic during the scheduled intravenous infusion of Carfilzomib (KRd treatment) (day 1 and 15 in each cycle) as described in table 1. In case of failure with the electronic equipment (e.g. tablet is out of power, wireless internet out of function, ect.) hard copies of the PRO questionnaires will be used to collect data.

Timing of PRO data collection

Collection of PRO data follows the scheduled visits as described in table 1. Therefore, if an otherwise scheduled KRd treatment is cancelled/rescheduled so will the collection of PRO data be. However, the responsible study nurse is required to report the reasons why the PRO assessment was not obtained as scheduled using the below options:

- Due to public holiday
- Due to side effects and/or treatment complications (e.g. concomitant pneumonia)
- Due to patient wish
- Other reason, please specify

If a scheduled treatment, and thus also the accompanying scheduled PRO data collection, is re-scheduled the responsible study nurse is required to report the number of days from the scheduled PRO data assessment and to the actual PRO data assessment, using the below options:

- 1-3 days
- 4-7 days
- 8-15 days
- 16-21 days

- 22-31 days
- 1-2 months
- >2 months

Actions to minimize missing data

If collection of PRO data is missed (for whatever reason) at the day of KRd treatment (day 1 and 15 in each cycle, table 1) alternative PRO completion methods will be used. The time window for completing QoL assessment in alternative ways is no more than 2 working days from the day that the scheduled QoL assessment was missed. This means, that if a QoL assessment is scheduled to be performed on a Tuesday, the alternative QoL assessment should be completed no later than Thursday the same week. The study nurse is required to try and contact/call the patient at least twice a day for two consecutive days from the scheduled PRO data collection that was missed.

The PRO data can be obtained alternatively as follows:

- According to the treatment schedule, the patient will be in for intravenous Carfilzomib treatment also at day 16 (the day after). The PRO data may then be collected electronically that day

OR

- The PRO data may be completed by telephone (study nurse complete the questionnaires (PRO data) through interview)

OR

- The PRO data may be collected through email (a PDF version of the PROs will be emailed to the patient. The patient complete the questionnaires within a maximum of two days from

the scheduled PRO data assessment. The patient returns the questionnaires to the study nurse at the next treatment visit)

If the patient cannot be reached or that the patient is unwilling to complete PRO data in alternative ways the collection of PRO data will be missed. The reasons why PRO data are missing is reported by the study nurse.

Monitoring of compliance with the PRO data

The QLR will monitor that the procedures above are followed. If not, the QLR contacts the study nurse responsible for the specific PRO data collection to make sure that procedures regarding future QoL assessments are followed.

Information on the Course of Treatment

The responsible study nurse is required to monitor the course of KRd treatment continously at day 1 and 15 in each cycle with regards to the use of diuretic and anti-hypertensive drug. If any of these medicaments are used by the patient the study nurse will register dose and frequency of intake within the last seven days from the KRd treatments at day 1 and 15. These informations will be used to interpret the health-related PRO scores obtained by the questionnaires through the course of KRd treatment.

Training of staff to collect PRO data

Online video material/guidelines on how to collect the PRO data and how to use the QoL eCRF is provided to the study nurses prior to inclusion of patients. Online material/guidelines are located at www.screencast-o-matic.com. Study nurses are encouraged to look through the material and also to upload at least one pilot patient into the QoL eCRF before enrollment of patients begins.

DATA MANAGEMENT

The PRO data will be stored on a secure server under the Region of Southern Denmark. The REDCap database (21) is used as platform for the PRO data, for which there also is a license agreement with Odense Patient Explorative Network (OPEN) at Odense University Hospital, Odense, Denmark. A data processor agreement is entered between the primary investigator and the Quality of Life Research Center, Odense University Hospital. This is to ensure that the rules of processing of personal data are followed at any given time point.

STATISTICAL CONSIDERATIONS

The present PRO protocol is not covered by sample size calculations for the main trial. The reporting of PRO data may thus only be describing/exploratory/hypothesis generating. However, by prespecifying PRO key domains and time points for primary analysis in the current PRO protocol risk of type 1 errors (multible statistical testing) is limited. Using PROs as described above, fluctuations in health-related QoL during the KRd treatment will be captured. Among other, comparison of health-related QoL scores between patients that are PET-CT positive and those that are PET-CT negative will be possible as well as changes in health-related QoL prior to and after recieving a PET-CT positive diagnose.

Scoring manuals from the EORTC QLQ-C30 and QLQ-CIPN20 besides FACT-PSI will be used to calculate sumscores for each of the instruments and their subscales. Demographic (age, gender) and clinical charactheristics (medical history, symptoms, performance status) will be derived from the CONPET eCRF clinical database.

A detailed statistical analysis plan (SAP) will be developed and made publicly available prior to the last included patient. Herein, handling of missing data as well as statistically methods used to analyse the PRO data will be described.

Primary PRO analysis time point

In each treatment cycle, “shortness of breath” will be analysed by comparing the FACT-PSI score on day 1 and 15 to the baseline FACT-PSI score. Due to the course of treatment higher FACT-PSI scores are expected at day 15 compared to day 1.

The primary analysis of peripheral neuropathy is prespecified to 1 month after the last day of cycle 4.

Primary analysis of global QoL is prespecified to 1 month after the last day of cycle 4.

APPENDICES

Appendices 1: Participant eligibility criteria for the CONPET trial

Appendices 2: EORTC QLQ-C30

Appendices 3: EORTC CIPN20

Appendices 4: FACT-PSI

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Appendices 1 (STUDY POPULATION)

9.1 Inclusion criteria

Each patient must meet all the following inclusion criteria to be enrolled in the study:

1. At least 18 years of age, with at least 6 months expected survival.

2. Prior confirmed diagnosis of multiple myeloma.

3. Received standard first line treatment with at least a very good partial response (VGPR). Standard first line treatment is defined as

    - VRD, VTD or VCD followed by ASCT

    - MPV at least 6 cycles, or no further reduction in monoclonal component the last 2 cycles, or

    - Rd at least 9 cycles or no further reduction in monoclonal component the last 2 cycles.

    - VRd at least 6 cycles or no further reduction in monoclonal component the last 2 cycles

4. Patients must be carfilzomib naive.

5. Successful FISH evaluation performed with available results.

6. Voluntary written consent must be given before performance of any study related procedure not part of standard medical care, with the understanding that the patient may withdraw consent at any time without prejudice to future medical care.

7. Females of childbearing potential (FCBPs) must have a confirmed negative serum pregnancy test within the 7 days prior to inclusion

8. FCBPs and male subjects who are sexually active with FCBP must agree to use highly effective concomitant methods of contraceptive during the study and for 30 days following the last study drug dose. Male subjects must use contraception and refrain from donating sperm for at least 90 days after the last dose of carfilzomib.

9. Eastern Cooperative Oncology Group (ECOG) performance status 0-2. In patients >75 years of age, performance status 0-1.

10. Patients must meet the following adequate organ and bone marrow function within 21 days prior to inclusion:

    • Absolute neutrophil count (ANC) $\geq$ 0,5 x 10^9/L) and platelet count 35 x 10^9/L. Platelet transfusions to help patients meet eligibility criteria are not allowed within 3 days before study enrollment. Granulocyte growth factors are allowed to meet the inclusion criteria.

11. Patient must be willing and able to adhere to the study schedule and other protocol requirements.

9.2 Exclusion criteria

Patients meeting any of the following exclusion criteria are not to be enrolled in the study:

1. Change of first line treatment because of stabile or progressive disease.
2. Female patients who are lactating or have a positive serum pregnancy test during the screening period.
3. Major surgery within 28 days before enrollment.
4. Radiotherapy within 14 days before enrollment.Glucocorticoid therapy within the 14 days prior to inclusion that exceeds a cumulative dose of 160 mg dexamethasone or 1000 mg prednisone.
5. Central nervous system involvement.
6. Uncontrolled heart disease, including congestive heart failure (NYHA III-IV), uncontrolled angina pectoris, uncontrolled conduction abnormalities, acute diffuse infiltrative pulmonary disease, pericardial disease or myocardial infarction within 6 months prior to enrollment
7. Active hepatitis B or C infection, or known human immunodeficiency virus (HIV) positivity.
8. Any other serious medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with the completion of treatment according to this protocol.
9. Known allergy to Captisol (a cyclodextrin derivative used to solubilize carfilzomib) or to any of the study medications, their analogues, or excipients in the various formulations of any agent.
10. Contraindication to dexamethasone or any of the required concomitant drugs or supportive treatments, including hypersensitivity to antiviral drugs, or intolerance to hydration due to pre-existing pulmonary or cardiac impairment.
11. Another active malignancy. Patients with non-melanoma skin cancer or carcinoma in situ of any type are not excluded if they have undergone complete resection.
12. Patients that have previously been treated with carfilzomib.
13. Primary plasma cell leukemia, systemic AL amyloidosis, Waldenströms macroglobulinemia, POEMS syndrome.
14. Pleural effusions requiring thoracocentesis within the 14 days prior the inclusion.
15. Ascites requiring ascites puncture within the 14 days prior to inclusion.
16. Previous allogeneic transplantation
17. Uncontrolled hypertension or uncontrolled diabetes despite medication
18. Contraindication to PET-CT

EORTC QLQ-C30 (version 3.0)

Vi er interesserede i at vide noget om dig og dit helbred. Vær venlig at besvare alle spørgsmålene selv ved at sætte en ring omkring det svar (tal), som passer bedst på dig. Der er ingen "rigtige" eller "forkerte" svar. De oplysninger, som du giver os, vil forblive strengt fortrolige.

Skriv venligst dine forbogstaver her:
Din fødselsdato (dag, måned, år):
Dato for udfyldelse af dette skema (dag, måned, år): 31

		Slet ikke	Lidt	En del	Meget
1.	Har du nogen vanskeligheder ved at udføre anstrengende aktiviteter, som f.eks. at bære en tung indkøbstaske eller en kuffert?	1	2	3	4
2.	Har du nogen vanskeligheder ved at gå en lang tur?	1	2	3	4
3.	Har du nogen vanskeligheder ved at gå en kort tur udendørs?	1	2	3	4
4.	Er du nødt til at ligge i sengen eller sidde i en stol om dagen?	1	2	3	4
5.	Har du brug for hjælp til at spise, tage tøj på, vaske dig eller gå på toilettet?	1	2	3	4

I den forløbne uge:

		Slet ikke	Lidt	En del	Meget
6.	Var du begrænset i udførelsen af enten dit arbejde eller andre daglige aktiviteter?	1	2	3	4
7.	Var du begrænset i at dyrke dine hobbyer eller andre fritidsaktiviteter?	1	2	3	4
8.	Havde du åndenød?	1	2	3	4
9.	Har du haft smerter?	1	2	3	4
10.	Havde du brug for at hvile dig?	1	2	3	4
11.	Har du haft søvnbesvær?	1	2	3	4
12.	Har du følt dig svag?	1	2	3	4
13.	Har du savnet appetit?	1	2	3	4
14.	Har du haft kvalme?	1	2	3	4
15.	Har du kastet op?	1	2	3	4
16.	Har du haft forstoppelse?	1	2	3	4

Vær venlig at fortsætte på næste side

I den forløbne uge:

	Slet ikke	Lidt	En del	Meget
17. Har du haft diarré (tynd mave)?	1	2	3	4
18. Var du træt?	1	2	3	4
19. Vanskeliggjorde smerter dine daglige gøremål?	1	2	3	4
20. Har du haft svært ved at koncentrere dig om ting som f.eks. at læse avis eller se fjernsyn?	1	2	3	4
21. Følte du dig anspændt?	1	2	3	4
22. Var du bekymret?	1	2	3	4
23. Følte du dig irritabel?	1	2	3	4
24. Følte du dig deprimeret?	1	2	3	4
25. Har du haft svært ved at huske?	1	2	3	4
26. Har din fysiske tilstand eller medicinske behandling vanskeliggjort dit familieliv?	1	2	3	4
27. Har din fysiske tilstand eller medicinske behandling vanskeliggjort din omgang med andre mennesker?	1	2	3	4
28. Har din fysiske tilstand eller medicinske behandling medført økonomiske vanskeligheder for dig?	1	2	3	4

Ved de næste 2 spørgsmål bedes du sætte en ring omkring det tal mellem 1 og 7, som passer bedst på dig

29. Hvordan vil du vurdere dit samlede helbred i den forløbne uge?

1 2 3 4 5 6 7

Meget dårligt Særdeles godt

30. Hvordan vil du vurdere din samlede livskvalitet i den forløbne uge?

1 2 3 4 5 6 7

Meget dårlig Særdeles god

EORTC QLQ-C30 (versjon 3.0.)

Vi er interessert i forhold vedrørende deg og din helse. Vær så vennlig å besvare hvert spørsmål ved å sette en ring rundt det tallet som best beskriver din tilstand. Det er ingen "riktige" eller "gale" svar. Alle opplysningene vil bli behandlet konfidensielt.

Ditt navns forbokstaver: _____

Født (dag, mnd, år): _____

Dato (dag, mnd, år): 31 _____

		Ikke i det hele tatt	Litt	En del	Svært mye
1.	Har du vanskeligheter med å utføre anstrengende aktiviteter, slik som å bære en tung handlekurv eller en koffert?	1	2	3	4
2.	Har du vanskeligheter med å gå en lang tur?	1	2	3	4
3.	Har du vanskeligheter med å gå en kort tur utendørs?	1	2	3	4
4.	Er du nødt til å ligge til sengs eller sitte i en stol i løpet av dagen?	1	2	3	4
5.	Trenger du hjelp til å spise, kle på deg, vaske deg eller gå på toalettet?	1	2	3	4

I løpet av den siste uken:

		Ikke i det hele tatt	Litt	En del	Svært mye
6.	Har du hatt redusert evne til å arbeide eller utføre andre daglige aktiviteter?	1	2	3	4
7.	Har du hatt redusert evne til å utføre dine hobbyer eller andre fritidsaktiviteter?	1	2	3	4
8.	Har du vært tung i pusten?	1	2	3	4
9.	Har du hatt smerter?	1	2	3	4
10.	Har du hatt behov for å hvile?	1	2	3	4
11.	Har du hatt søvnproblemer?	1	2	3	4
12.	Har du følt deg slapp?	1	2	3	4
13.	Har du hatt dårlig matlyst?	1	2	3	4
14.	Har du vært kvalm?	1	2	3	4

Bla om til neste side

I løpet av den siste uken:

		Ikke i det hele tatt	Litt	En del	Svært mye
15.	Har du kastet opp?	1	2	3	4
16.	Har du hatt treg mage?	1	2	3	4
17.	Har du hatt løs mage?	1	2	3	4
18.	Har du følt deg trett?	1	2	3	4
19.	Har smerter påvirket dine daglige aktiviteter?	1	2	3	4
20.	Har du hatt problemer med å konsentrere deg, f.eks. med å lese en avis eller se på TV?	1	2	3	4
21.	Har du følt deg anspent?	1	2	3	4
22.	Har du vært engstelig?	1	2	3	4
23.	Har du følt deg irritabel?	1	2	3	4
24.	Har du følt deg deprimert?	1	2	3	4
25.	Har du hatt problemer med å huske ting?	1	2	3	4
26.	Har din fysiske tilstand eller medisinske behandling påvirket ditt familieliv?	1	2	3	4
27.	Har din fysiske tilstand eller medisinske behandling påvirket dine sosiale aktiviteter?	1	2	3	4
28.	Har din fysiske tilstand eller medisinske behandling gitt deg økonomiske problemer?	1	2	3	4

Som svar på de neste spørsmålene, sett en ring rundt det tallet fra 1 til 7 som best beskriver din tilstand

29. Hvordan har din helse vært i løpet av den siste uken?

1	2	3	4	5	6	7
Svært dårlig						Helt utmerket

30. Hvordan har livskvaliteten din vært i løpet av den siste uken?

1	2	3	4	5	6	7
Svært dårlig						Helt utmerket

EORTC QLQ-C30 (version 3)

Vi är intresserade av några saker som har med dig och din hälsa att göra. Besvara alla frågor genom att sätta en ring runt den siffra som stämmer bäst in på dig. Det finns inga svar som är "rätt" eller "fel". Den information du lämnar kommer att hållas strikt konfidentiell.

Fyll i Dina initialer: ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

När är Du född? (Dag, Månad, År): ⌊ ⌋⌊ ⌋ ⌊ ⌋⌊ ⌋ ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

Dagens datum (Dag, Månad, År): 31 ⌊ ⌋⌊ ⌋ ⌊ ⌋⌊ ⌋ ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

		Inte alls	Lite	En hel del	Mycket
1.	Har du svårt att göra ansträngande saker, som att bära en tung kasse eller väska?	1	2	3	4
2.	Har du svårt att ta en lång promenad?	1	2	3	4
3.	Har du svårt att ta en kort promenad utomhus?	1	2	3	4
4.	Måste du sitta eller ligga på dagarna?	1	2	3	4
5.	Behöver du hjälp med att äta, klä dig, tvätta dig eller gå på toaletten?	1	2	3	4

Under veckan som gått:

		Inte alls	Lite	En hel del	Mycket
6.	Har du varit begränsad i dina möjligheter att utföra antingen ditt förvärvsarbete eller andra dagliga aktiviteter?	1	2	3	4
7.	Har du varit begränsad i dina möjligheter att utöva dina hobbyer eller andra fritidssysselsättningar?	1	2	3	4
8.	Har du blivit andfådd?	1	2	3	4
9.	Har du haft ont?	1	2	3	4
10.	Har du behövt vila?	1	2	3	4
11.	Har du haft svårt att sova?	1	2	3	4
12.	Har du känt dig svag?	1	2	3	4
13.	Har du haft dålig aptit?	1	2	3	4
14.	Har du känt dig illamående?	1	2	3	4
15.	Har du kräkts?	1	2	3	4
16.	Har du varit förstoppad?	1	2	3	4

Fortsätt på nästa sida

Under veckan som gått:		**Inte alls**	**Lite**	**En hel del**	**Mycket**
17.	Har du haft diarré?	1	2	3	4
18.	Har du varit trött?	1	2	3	4
19.	Har dina dagliga aktiviteter påverkats av smärta?	1	2	3	4
20.	Har du haft svårt att koncentrera dig, t.ex. läsa tidningen eller se på TV?	1	2	3	4
21.	Har du känt dig spänd?	1	2	3	4
22.	Har du oroat dig?	1	2	3	4
23.	Har du känt dig irriterad?	1	2	3	4
24.	Har du känt dig nedstämd?	1	2	3	4
25.	Har du haft svårt att komma ihåg saker?	1	2	3	4
26.	Har ditt fysiska tillstånd eller den medicinska behandlingen stört ditt familjeliv?	1	2	3	4
27.	Har ditt fysiska tillstånd eller den medicinska behandlingen stört dina sociala aktiviteter?	1	2	3	4
28.	Har ditt fysiska tillstånd eller den medicinska behandlingen gjort att du fått ekonomiska svårigheter?	1	2	3	4

Sätt en ring runt den siffra mellan 1 och 7 som stämmer bäst in på dig för följande frågor:

29. Hur skulle du vilja beskriva din hälsa totalt sett under den vecka som gått?

1	2	3	4	5	6	7
Mycket dålig						Utmärkt

30. Hur skulle du vilja beskriva din totala livskvalitet under den vecka som gått?

1	2	3	4	5	6	7
Mycket dålig						Utmärkt

EORTC QLQ – CIPN20

Patienter fortæller undertiden, at de har følgende symptomer eller problemer. Anfør venligst, i hvilket omfang du har haft disse symptomer eller problemer inden for den forløbne uge. Besvar spørgsmålene ved at sætte en ring omkring det tal, som passer bedst til dig.

I den forløbne uge:	**Slet ikke**	**Lidt**	**En del**	**Meget**
31. Har du haft en prikkende fornemmelse i fingre eller hænder?	1	2	3	4
32. Har du haft en prikkende fornemmelse i tæer eller fødder?	1	2	3	4
33. Har du været følelsesløs i fingre eller hænder?	1	2	3	4
34. Har du været følelsesløs i tæer eller fødder?	1	2	3	4
35. Har du haft en jagende eller brændende smerte i fingre eller hænder?	1	2	3	4
36. Har du haft en jagende eller brændende smerte i tæer eller fødder?	1	2	3	4
37. Har du haft kramper i dine hænder?	1	2	3	4
38. Har du haft kramper i dine fødder?	1	2	3	4
39. Har du haft problemer med at stå eller gå på grund af besvær med at mærke underlaget under dine fødder?	1	2	3	4
40. Har du haft svært ved at skelne mellem varmt og koldt vand?	1	2	3	4
41. Har du haft problemer med at skrive fordi du ikke kunne holde ordentligt på en blyant eller en kuglepen?	1	2	3	4
42. Har du haft svært ved at håndtere små ting med dine fingre (f.eks. knappe små knapper)?	1	2	3	4
43. Har du haft svært ved at åbne syltetøjsglas eller flasker fordi du manglede kræfter i hænderne?	1	2	3	4
44. Har du haft svært ved at gå, fordi du har en drop-fod (fordi du ikke kan bøje din fod opad)?	1	2	3	4

Vær venlig at fortsætte på næste side

I den forløbne uge:	Slet ikke	Lidt	En del	Meget
45. Har du haft svært ved at gå opad trapper eller rejse dig fra en stol fordi du manglede kræfter i dine ben?	1	2	3	4
46. Har du været svimmel efter at du rejste dig fra siddende eller liggende stilling?	1	2	3	4
47. Har du haft sløret syn?	1	2	3	4
48. Har du haft besvær med at høre?	1	2	3	4

Besvar venligst kun følgende spørgsmål, hvis du kører bil:

49. Har du haft besvær med at betjene pedalerne?	1	2	3	4

Besvar venligst kun følgende spørgsmål, hvis du er en mand:

50. Har du haft problemer med at få eller bevare en erektion?	1	2	3	4

EORTC QLQ-CIPN20

En del pasienter opplever av og til at de har noen av følgende symptomer eller problemer. Vær vennlig å angi i hvilken grad du har hatt disse symptomene eller problemene i løpet av den siste uka. Sett en ring rundt det tallet som best beskriver din tilstand.

I løpet av den siste uka:	**Ikke i det hele tatt**	**Litt**	**En del**	**Svært mye**
31. Har du hatt kribling i fingre eller hender?	1	2	3	4
32. Har du hatt kribling i tær eller føtter?	1	2	3	4
33. Har du hatt nummenhet i fingre eller hender?	1	2	3	4
34. Har du hatt nummenhet i tær eller føtter?	1	2	3	4
35. Har du hatt ilende eller brennende smerte i dine fingre eller hender?	1	2	3	4
36. Har du hatt ilende eller brennende smerte i dine tær eller føtter?	1	2	3	4
37. Har du hatt kramper i dine hender?	1	2	3	4
38. Har du hatt kramper i dine føtter?	1	2	3	4
39. Har du hatt problemer med å stå eller gå p.g.a. vanskeligheter med å føle bakken under dine føtter?	1	2	3	4
40. Har du hatt vanskelig for å skille mellom varmt og kaldt vann?	1	2	3	4
41. Har du hatt vanskeligheter med å skrive p.g.a. at du har hatt problemer med å holde en penn?	1	2	3	4
42. Har du hatt vanskeligheter med å håndtere små gjenstander med fingrene (f. eks. kneppe små knapper)?	1	2	3	4
43. Har du hatt vanskeligheter med å åpne et glass med skrukork eller en flaske p.g.a. kraftløshet i hendene?	1	2	3	4
44. Har du hatt vanskeligheter med å gå p.g.a. at føttene dine falt nedover (droppfot)?	1	2	3	4

Bla om til neste side

I løpet av den siste uka:	**Ikke i det hele tatt**	**Litt**	**En del**	**Svært mye**
45. Har du hatt vanskeligheter med å gå i trapper eller reise deg fra en stol p.g.a. kraftløshet i bena?	1	2	3	4
46. Har du blitt svimmel når du har reist deg fra en sittende eller liggende stilling?	1	2	3	4
47. Har du hatt uklart syn?	1	2	3	4
48. Har du hatt vanskelig for å høre?	1	2	3	4
Vennligst svar på følgende spørsmål kun dersom du kjører bil:				
49. Har du hatt vanskeligheter med å bruke pedalene?	1	2	3	4
Vennligst svar på følgende spørsmål kun dersom du er mann:				
50. Har du hatt vanskeligheter med å få eller opprettholde en ereksjon?	1	2	3	4

EORTC QLQ – CIPN20

Patienter berättar ibland att de har följande symtom eller problem. Markera i vilken utsträckning som du har haft dessa symptom eller problem under den senaste veckan. Svara genom att ringa in den siffra som bäst passar in på dig.

Under veckan som gått:		**Inte alls**	**Lite**	**En hel del**	**Mycket**
31.	Har du haft stickningar i fingrar eller händer?	1	2	3	4
32.	Har du haft stickningar i tår eller fötter?	1	2	3	4
33.	Har du haft domningar i fingrar eller händer?	1	2	3	4
34.	Har du haft domningar i tår eller fötter?	1	2	3	4
35.	Har du haft ilande eller brännande smärta i fingrar eller händer?	1	2	3	4
36.	Har du haft ilande eller brännande smärta i tår eller fötter?	1	2	3	4
37.	Har du haft kramp i händerna?	1	2	3	4
38.	Har du haft kramp i fötterna?	1	2	3	4
39.	Har du haft problem med att stå eller gå på grund av att det var svårt att känna underlaget under fötterna?	1	2	3	4
40.	Har du haft svårt att känna skillnaden mellan varmt och kallt vatten?	1	2	3	4
41.	Har du haft problem med att hålla i en penna och därmed haft svårt att skriva?	1	2	3	4
42.	Har du haft svårt att hantera små föremål med fingrarna (t.ex. att knäppa små knappar)?	1	2	3	4
43.	Har du haft svårt att öppna en burk eller flaska på grund av svaghet i händerna?	1	2	3	4
44.	Har du haft svårt att gå på grund av droppfot (som om framfoten faller framåt)?	1	2	3	4

Fortsätt på nästa sida.

Under veckan som gått:		**Inte Alls**	**Lite**	**En hel del**	**Mycket**
45.	Har du haft svårt att gå uppför trappor eller att resa dig från en stol på grund av svaghet i benen?	1	2	3	4
46.	Har du känt yrsel då du stigit upp från sittande eller liggande ställning?	1	2	3	4
47.	Har du haft dimsyn?	1	2	3	4
48.	Har du haft svårt att höra?	1	2	3	4

Besvara följande fråga endast om du kör bil:

49.	Har du haft svårt att använda pedalerna?	1	2	3	4

Besvara följande fråga endast om du är en man:

50.	Har du haft svårt att få eller bibehålla en erektion?	1	2	3	4

PSI (Version 4)

Nedenfor er anført en række udsagn, som andre mennesker med din sygdom har sagt, er vigtige.
Ved at sætte en ring omkring ét af tallene i hver linie, bedes du angive, hvor sandt hvert enkelt udsagn har været for dit vedkommende i løbet af de sidste 7 dage.

		Slet ikke	En lille smule	I nogen grad	En hel del	Meget
B1	Jeg bliver let forpustet.....	0	1	2	3	4
L2	Jeg har hostet.....	0	1	2	3	4
L3	Jeg har trykken i brystet	0	1	2	3	4
L4	Jeg har let ved at trække vejret.....	0	1	2	3	4

PSI (Versjon 4)

Nedenfor finner du en liste med uttalelser som andre mennesker med samme sykdom som deg mener er av betydning. **Sett ring rundt eller merk av ett tall per linje for å angi svaret ditt, slik det gjelder for de siste 7 dagene.**

		Ikke i det hele tatt	Litt	Til en viss grad	Mye	Svært mye
B1	Jeg har vært kortpustet	0	1	2	3	4
L2	Jeg hoster.....	0	1	2	3	4
L3	Jeg føler stramming i brystet.....	0	1	2	3	4
L4	Jeg kan puste uten vanskeligheter	0	1	2	3	4

PSI (Version 4)

Nedan finner du en lista med uttalanden som andra människor med din sjukdom tycker är viktiga. **Ringa in eller markera en siffra per rad för att ange ditt svar som ska gälla de <u>senaste 7 dagarna</u>.**

		Inte alls	En aning	Något	Ganska mycket	Väldigt mycket
B1	Jag har varit andfådd	0	1	2	3	4
L2	Jag har hostat	0	1	2	3	4
L3	Jag känner tryck över bröstet	0	1	2	3	4
L4	Jag har lätt för att andas.....	0	1	2	3	4